Entry of this amendment is respectfully requested. The specification has been amended to include a Sequence Listing and appropriate reference to the sequences therein. The amendments are made in adherence with 37 C.F.R. § 1.821-1.825. This amendment is accompanied by a floppy disk containing the above named sequence, SEQUENCE ID NUMBERS 1-36, in computer readable form, and a paper copy of the sequence information. The computer readable sequence listing was prepared through use of the software program "PatentIn" provided by the PTO. The information contained in the computer readable disk is identical to that of the paper copy. This amendment contains no new matter. Applicant submits that this amendment, the accompanying computer readable sequence listing, and the paper copy thereof serve to place this application in a condition of adherence to the rules 37 C.F.R. § 1.821-1.825.

Please direct any calls in connection with this application to the undersigned at (415) 781-1989.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

Paragraph beginning at page 3, line 16, has been amended as follows:

– In one aspect, a recombinant nucleic acid encoding a cell cycle protein of the present invention comprises a nucleic acid that hybridizes under high stringency conditions to a sequence complementary to that set forth in Figure 21, 22, 23, 24, 25, 26, 27 or 28 (SEQ ID NOS:1-8). In a preferred embodiment, the cell cycle protein provided herein binds to Traf2 or Nck. Most preferably, the cell cycle protein binds to Traf2 and binds to Nck.–

Paragraph beginning at page 3, line 21, has been amended as follows:

– In one embodiment, a recombinant nucleic acid is provided which comprises a nucleic acid sequence as set forth in Figure 21, 22, 23, 24, 25, 26, 27 or 28 (SEQ ID NOS:1-8). In another embodiment, a recombinant nucleic acid encoding a cell cycle protein is provided which comprises a nucleic acid sequence having at least 85% sequence identity to a sequence as set forth in Figure 21, 22, 23, 24, 25, 26, 27 or 28. In a further embodiment, provided herein is a recombinant nucleic acid encoding an amino acid sequence as depicted in Figure 1 for Tnik (SEQ ID NO:34), or Figure 29, 30, 31, 32, 33, 34 or 35 (SEQ ID NOS:9-15). –

Paragraph beginning at page 4, line 3, has been amended as follows:

– Also provided herein are recombinant cell cycle proteins encoded by the nucleic acids of the present invention. In one aspect, a recombinant polypeptide is provided herein which comprises an amino acid sequence having at least 80% sequence identity with a sequence as set forth in Figure 21, 22, 23, 24, 25, 26, 27 or 28 (SEQ ID NOS:1-8). In one embodiment, a recombinant cell cycle protein is provided which comprises an amino acid sequence as set forth in Figure 1 for Tnik (SEQ ID NO:34), or Figure 29, 30, 31, 32, 33, 34 or 35 (SEQ ID NOS:9-15). –

Paragraph beginning at page 4, line 32, has been amended as follows:

– Figure 1 shows a sequence alignment of Tnik (top sequence; SEQ ID NO:34) to NIK (bottom sequence; SEQ ID NO:35). Identical residues are shaded with black and homologous residues are shaded with gray and dotted below. The three alternatively spliced exons are marked by (–) above the Tnik sequence. –

Paragraph beginning at page 10, line 31, has been amended as follows:

– In one embodiment, the cell cycle protein has one or more of the following characteristics: an intermediate region which shares greater than 40%, more preferably greater than 65%, more preferably, greater than 75%, more preferably greater than 85%, more preferably greater than 95% homology to the corresponding amino acids as shown in Figure 1 (SEQ ID NOS:34-35) or encoded by any of the nucleic acids of Figures 21-28 (SEQ ID NOS:1-8); an N-terminal kinase domain of the cell cycle protein which shares greater than 90%, more preferably 95% homology to the corresponding amino acids as shown in Figure 1 or encoded by any one of the nucleic acids of Figures 21-28; a C-terminal ~~genminal~~ germinal center kinase homology region which has greater than 90%, more preferably 95% homology to the corresponding amino acids as shown in any one of Figures 1 and 29-35 (SEQ ID NOS:9-15). The embodiments provided herein explicitly include any combination of these characteristics. Moreover, the homology of the cell cycle protein may be greater in one region corresponding to one or more of the isoforms but not the other. –

Paragraph beginning at page 11, line 18, has been amended as follows:

– In a preferred embodiment, a protein is a "cell cycle protein" as defined herein if the overall sequence identity of the amino acid sequence of Figure 1 for Tnik (SEQ ID NO:34), or Figure 29, 30, 31, 32, 33, 34 or 35 (SEQ ID NOS:9-15) is preferably greater than about 75%, more preferably greater than about 80%, even more preferably greater than about 85% and most preferably greater than 90%. In some embodiments the sequence identity will be as high as about 93 to 95 or 98%. –

Paragraph beginning at page 11, line 23, has been amended as follows:

– In another preferred embodiment, a cell cycle protein has an overall sequence similarity with the amino acid sequence of Figure 1 for Tnik (SEQ ID NO:34), or Figure 29, 30, 31, 32, 33, 34 or 35 (SEQ ID NOS:9-15), of greater than about 80%, more preferably greater than about 85%, even more preferably greater than about 90% and most preferably greater than 93%. In some embodiments the sequence identity will be as high as about 95 to 98 or 99%. –

Paragraph beginning at page 43, line 8, has been amended as follows:

– A number of cyclin destruction boxes are known in the art, for example, cyclin A has a destruction box comprising the sequence RTVLGVIGD (SEQ ID NO:16); the destruction box of cyclin B1 comprises the sequence RTALGDIGN (SEQ ID NO:17). See Glotzer, et al., Nature, 349:132-138 (1991). Other destruction boxes are known as well: YMTVSIIDRFMQDSCVPKKMLQLVGVT (rat cyclin B; SEQ ID NO:18); KFRLLQETMYMTVSIIDRFMQNSCVPKK (mouse cyclin B; SEQ ID NO:19); RAILIDWLIQVQMKFRLLQETMYMTVS (mouse cyclin B1; SEQ ID NO:20); DRFLQAQLVCRKKLQVVGITALLLASK (mouse cyclin B2; SEQ ID NO:21); and MSVLRGKLQLVGTAAMLL (mouse cyclin A2; SEQ ID NO:22). –

Paragraph beginning at page 58, line 16, has been amended as follows:

– *Cloning of full length Tnik and Northern blotting* - Using yeast two-hybrid screening, overlapping cDNA fragments were identified that interacted with Traf2 and NCK. The sequences of the fragments were contained in a partial cDNA clone, KIAA0551 (Accession number AB011123), at GenBank. Antisense oligos TGCGCTTATATTCCAGAAGTAGAGCT (SEQ ID NO:23) and CTGTCTCTGCTCCTCCTCTA (SEQ ID NO:24) were designed according to the 5' end sequence of KIAA0551 and the full length Tnik cDNA was cloned from reverse transcribed human brain mRNA by RACE-PCR. Northern blotting was performed on human multi-tissue Northern blot according to the manufacturer's recommendations (Clontech). A PCR product amplified from nucleotide 1264 to nucleotide 2427 of Tnik coding region was used as a probe. –

Paragraph beginning at page 58, line 25, has been amended as follows:

– *Plasmid construction* – Full length human Tnik was cloned into pCI (Promega) derived expression vector pYCI under the control of the CMV promoter with an HA epitope tag (AYPYDVPDYA; SEQ ID NO:25) inserted on the N-terminus by PCR. A kinase mutant form of Tnik was constructed using the QuikChange mutagenesis kit (Stratagene) with Oligos AGCTTGCAGCCATCAGGGTTATGGATGTCAC (SEQ ID NO:26) and GTGACATCCATAACCTTGATGGCTGCAAGCT (SEQ ID NO:27) to change the highly conserved lysine 54 in the kinase domain to arginine. Full length human Traf2 was cloned into pYCI with a FLAG epitope tag (DYKDDDDKG; SEQ ID NO:28) inserted on the N-terminus by PCR. Full length human NCK was similarly cloned into pYCI with a FLAG epitope tag at the N-terminus. Myc-JNK2 and Myc-ERK1 were constructed in the pCR3.1 vector with a Myc epitope tag (ASMEQKLISEEDLN; SEQ ID NO:29) inserted on the N-terminus of JNK2 and ERK1, respectively. All the truncation mutants were constructed by PCR. For construction of the GFP-Tnik fusion protein, full length Tnik was PCR amplified from pYCI-Tnik and inserted in frame onto the 3'end of GFP. All constructs were verified by DNA sequencing. –

Paragraph beginning at page 64, line 26, has been amended as follows:

– NIK was cloned by its ability to interact with the adapter protein NCK. It associated with NCK SH3 domains via two PxxPxR sequences in the intermediate domain, PCPPSR (aa 574-579; SEQ ID NO:30) and PRVPVR (aa 611-616; SEQ ID NO:31). Both sequences were required for efficient interaction (Su, et al., EMBO J., 16:1279-1290 (1997)). Similar to NIK, Tnik also interacted with NCK via the intermediate domain. However, PCPPSR is not conserved in Tnik. Instead, Tnik contained two other PxxPxR sequences, PNLPPR (aa 562-567; SEQ ID NO:32) and PPLPTR (aa 647-652; SEQ ID NO:36), in addition to the conserved PKVPQR (aa 670-675; SEQ ID NO:33). Tnik likely interacted with NCK through the cooperative interaction with these three PxxPxR sequences. NCK is an adapter protein involved in many growth factor receptor mediated

signal transduction pathways (McCarthy, Bioessays, 20:913-921 (1998)). It has been proposed that the NIK-NCK interaction may recruit NIK to receptor or non-receptor tyrosine kinases to regulate MEKK1 (Su, et al., EMBO J., 16:1279-1290 (1997)). Tnik may be recruited in a similar fashion. –

On page 67, immediately preceding the heading "CLAIMS," the enclosed text entitled "SEQUENCE LISTING" was inserted into the text.